Acute Dystonia in a Child Receiving Metoclopramide: Case Report

Metoklopramid Alan Bir Çocukta Akut Distoni: Olgu Sunumu

Metoclopramide Side Effects

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Özet

Metoklopramid, dopamin reseptör antagonisti bir benzamid olup, gastroözefagial reflü hastalığının tedavisinde gastrointestinal pasajı hızlandırmak için prokinetik bir ajan olarak ve bulantı-kusma ile seyreden birçok hastalıkta antiemetik olarak sıklıkla tercih edilir. Sindirim sistemi üzerine hem santral hem de periferik etkilidir. Kan-beyin engelini kolayca aşar ve ekstrapiramidal sisteme ait yan etkiler oluşturabilir. Bu yan etkileri arasında akut distonik reaksiyon nadirdir ancak acil tedavi gerektiren bir durumdur. Bu yazıda yüksek dozda metpamid kullanımına bağlı akut distonik reaksiyon gelişen 5 aylık infant hastayı sunduk. Sunulan vakada tanı, öykü ile konuldu. Difenhidramin tedavisi ile hastanın şikâyetleri hızlıca ortadan kayboldu. Akut distoni ile acil servise başvuran hastalarda metoklopramidin yan etkisinin olabileceği unutulmamalı ve bu durumda hastalarda mutlaka ilaç kullanım öyküsü sorgulanmalıdır.

Anahtar Kelimeler

Akut Distoni; Çocuk; Metoklopramid

Abstract

Metoclopramide is a benzamide that is a dopamine receptor, often preferred as a prokinetic agent to accelerate gastrointestinal passage in the treatment of gastroesophageal reflux disease; itis also used as an antiemetic agent in many diseases that progress with nausea-vomiting. It is effective on the digestive system both centrally and peripherally. It easily overcomes the blood-brain barrier and may create side effects pertaining to the extrapyramidal system. Acute dystonic reaction is rare among these side effects; it is, however, a condition that needs to be treated urgently. This paper presents a 5-month-old infant patient who developed acute dystonic reaction secondary to the use of Metpamid at a high dose. The diagnosis in this case was made based onpatient history. The patient's symptoms rapidly disappeared thanks to treatment with diphenhydramine. It should be remembered that metoclopramide may cause side effects in patients presenting to the emergency service with acute dystonia, soa complete history of drugs should definitely be taken for such patients.

Keywords

Acute Dystonia; Child; Metoclopramide

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Introduction

Normal delivery in the central nervous system is enabled by the balance between dopaminergic and cholinergic receptors. Drugs such as antipsychotics, antiemetics, antihistaminics, decongestants, and expectorants may result in dystonic reactions by disrupting this balance, even at treatment doses [1]. It is known that metoclopramide is the drug that most often causes dystonic reaction among antiemetic drugs.Acute dystonic reaction, which is a neurological picture characterized by strong, repetitive, twisting and twirling muscle contractions and temporary or permanent bad posture, presents itself as contractions especially in muscles of the face, neck, and back as well as opisthotonus, torticollis, oculogyric crisis, dysarthria, and trismus [2]. Although rare, since the spasm of pharyngeal and laryngeal muscles may result in respiratory trouble, extrapyramidal symptoms that start acutelyduring the childhood period are considered medical emergencies and need to be treated immediately. Diagnosis is made based on the sudden onset of signs, its rapid progress, and inquiry into the history of drug use. In this case report, a 5-month-old female patient developed an acute dystonic reaction following high-dose metoclopramide treatment at the emergency service. The aim is to emphasize the requirement to inquire about the use of drugs that lead to extrapyramidal symptoms such as metoclopramide following neurological examination in cases that present with acute dystonic reaction.

Case Report

A 5-month-old female patient presented to the outpatient clinic of our hospital with the symptoms of nausea-vomiting and diarrhea. The patient was evaluated and her overall condition was moderate-good, weak and dehydrated. Her bodyweight was 6,9 kg (25-50 p), height 65 cm (25-50 p), head circumference 43 cm (25-50 p), body temperature 36,5 C, pulse 140/min, and TA 85/50 mmHg. Her physical examination results were normal other than the dryness identified in the tongue and mucosae and increased bowel sounds. It was noted that the patient had experienced projectile vomiting as well as yellow, mucous, foul-smelling diarrhea without blood six to seven times a day. It was learned that these symptoms had been present for 2 days and that she had been administered intravenous (IV) solution at another hospital where she was taken for these symptoms; however, her symptoms persisted. There were no unusual or pertinent traits in the patient's personal and family histories. It was learned that the patient, who seemed dehydrated, had received intravenous administration of IV solution and metoclopramide 7 mg/kg (5 mg). Approximately one hour after the administration, symptoms of tilting her head backwards and having her eyes cast upward were observed. Since the patient's symptoms did not abate in the follow-up period, it was decided to hospitalize her at the pediatric service for further studies and treatment. According to the general examination conducted at the pediatric unit, her overall condition was moderate-good, she was conscious, cooperative, oriented, and had a pale complexion. She had no pathological findings apart from having eyes cast upward, torticollis, opisthotonus, anddryness of the tongue and mucosae. The patient's laboratory study results were normal and it was considered that the acute dystonic reaction was associated with the administration of metoclopramide based on the information from the examination and anamnesis. She received IV administration of solution and biperiden lactate 1 mg. Since there were no improvements in the patient's clinical condition, the drug was re-administered at the same dose 1 hour later. The patient's clinical symptoms remained persistent; therefore, she received IV administration of diphenhydramine at a dose of 1 mg/kg. It was observed that the dystonic reaction signs of our patient completely disappeared 1 hour later. The patient was monitored for one day and discharged as cured.

Discussion

Metoclopramide is a selective dopamine receptor (D2R) antagonist with central and peripheral effects [1]. It makes tissues sensitive to the effects of acetylcholine, thereby increasing the movements of the upper digestive system. It especially increases the tonus and severity of contractions in the gastric antrum and intestinal movements in the duodenum and jejunum while it relaxes the pyloric sphincter and duodenal bulb.For that reason, it is used as a prokinetic agent to accelerate the emptying of the stomach and passage of food through the intestines in cases of dyspeptic symptoms secondary to digestive system motility disorders and gastrointestinal reflux disease [1]. Furthermore, it is also used in overcoming the symptoms of nausea-vomiting as a dopamine receptor antagonist. It is an antiemetic agent that has both central and peripheral effects on the digestive system. Its effects become apparent 1-3 minutes after intravenous administration, 10-15 minutes after intramuscular administration, and 30-60 minutes after oral intake. When it is taken orally, it is absorbed very rapidly and almost entirely through the gastrointestinal system. Its plasma concentration peaks within approximately 1-2 hours after the administration of an oral dose [3]. As it is significantly eliminated in its first passage through the liver and the rate of elimination in the liver varies among individuals, its bioavailability varies per person as well. It has a half-life of 5-6 hours in a person with normal renal functions. It is metabolized in the liver and excreted into urine. For that reason, dose adjustment should be performed in cases of hepatic and renal failure [4]. It also freely passes through the placenta and reaches 60-70% of its maternal plasma concentration in fetal plasma [3]. Regardless of whether it is administered at a normal or toxic dose, the period of emergence for its side effects is the first 24-72 hours after exposure to drug. Similarly, in our case, the symptoms emerged at approximately 1 hour following drug intake, in keeping with the literature. While the pediatric dose that is accepted for therapeutic purposeis 0.5mg/kg/day (administered in divided doses), the maximum tolerable dose range is reported to be 3.3-3.7mg/kg/day [5]. It was identified that our patient received a high dose of 7mg/kg as a result of an administration error.

Metoclopramide easily overcomes the blood-brain barrier and may result in disorders pertaining to the extrapyramidal system (acute dystonic reactions especially in children).It shows these effects by blocking the dopamine receptor (D2R) and stimulating the acetylcholine receptors found in the stomach muscle [6]. The resultant movement disabilities include Parkinsonism, tardive dyskinesia (involuntary movements), dystonic reactions (opisthotonus, torticollis, oculogyric crisis, dysarthria, trismus,

etc.), and neuroleptic malignant syndrome. Although the exact reason for anoculogyric crisis is not entirely known, it may be due to the contraction of extraocular muscles. An upwards spasmodic deviation of the eyes is often observed.

Although the incidence rate of signs secondary to the use of metoclopramide has been reported as 0.5-1% among adults, this rate may be as high as 25% among the elderly and children [7]. It has been reported to be more frequent in patients with a history of neurological disease in their family. Our patient was a 5-month-old female infant with no known neurological diseases in her family history.

The drug-related side effect of metoclopramideis not dose-dependent and may emerge idiosyncratically. For that reason, side effects may be seen even in treatment levels of doses. However, it has been reported that side effects develop more often when the recommended dose is exceeded and that repeated doses result in an accumulative effect [4]. Especially, tardive dyskinesia and Parkinsonism may develop due to high-dose or chronic administration of metoclopramide. On the other hand, Bateman et al. reported that the development of acute dystonic reaction secondary to metoclopramide is not associated with drug plasma concentration [2]. Additionally, Cezard et al. examined 81 cases that developed metoclopramide-related adverse drug reactions(ADR) and reported that sex and dose-effect correlationswere not effective in the emergence of side effects [8]. Furthermore, it is stated that the development of acute dystonic reaction secondary to metoclopramide may be familial since metoclopramide-related extrapyramidal side effects were reported in four cases in two families. In that regard, it is recommended that metoclopramide should not be administered to other individuals of the same family if one family member has a history of dystonia. Another study demonstrated that two patients who developed acute dystonic reaction following metoclopramide had homozygous cytochrome P450 2D6 gene polymorphism [6]. Metoclopramide is inhibited by hepatic cytochrome P450 enzyme subgroup CYP2D6. The extrapyramidal symptoms induced by drugs are seen more often in patients with genetic polymorphism in the site of gene CYP2D6, which results in loss of enzyme activity. In cases where there are nobetter alternatives to metoclopramide for persons at risk of extrapyramidal symptoms, non-functional CYP2D6 may be investigated before administering this drug [6].

Determining whether acute dystonic reaction developed secondary to metoclopramide may be difficult in cases where it is not considered to be a potential side effect of the drug and it may therefore be confounded with some other diseases. Patients may be misdiagnosed with conditions such as meningitis, encephalitis, hypocalcemia and hypomagnesemia, epilepsy, hysteria, scorpion sting and bug bite, food poisoning, or tetanus. Since our patient had a sudden onset of symptoms, she was conscious, cooperative and oriented, she did not have fever, her symptoms started suddenly and progressed rapidly, she did not have history of any disease, she did not have history of any drugs other than metoclopramide in her personal history, and her laboratory study results were normal and she responded quickly to the treatment administered, it was considered that her current dystonia picture was a side effect of metoclopramide. Other possible causes of dystonia were not considered in differential diagnosis. For patients who are brought to the pediatric emergency outpatient clinic with acute dystonia, central nervous system diseases such as encephalitis are most frequently considered and traumatic studies such as spinal tap are often performed for differential diagnosis of such diseases. Yis et al. reported that of two pediatric patientswho developed acute dystonia secondary to metoclopramide, one was initially hospitalized with the diagnosis of encephalitis and the other with tetany [4].

Diphenhydramine (1-2 mg/kg oral, IV or IM) or biperiden (2.5-5 mg IV or IM) are used for the treatment of acute dystonic reactions. Diazepam can be used in resistant cases. Biperiden 1 mg IV was used in our case. However, the drug was administered again at the same dose 1 hour later since there was no treatment response. As there was still no improvement in the patient's clinical condition, diphenhydramine at a dose of 1 mg/kg was intravenously administered; 1 hour after that, it was observed that the signs of dystonic reaction signs completely disappeared.

In conclusion, it is important to emphasize that physicians need to meticulously calculate the drug dose while prescribing drugs to pediatric patients and to explain any potential side effects to the caregivers. Furthermore, in patients presenting to the pediatric emergency outpatient clinic with an acute dystonic reaction, it is essential to take a completehistory of drug use and to carefully conduct the physical examination with respect to other accompanying neurological signs.

Competing interests

The authors declare that they have no competing interests.

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